Amendments to the Specification:

Please replace the paragraph beginning at page 2, line 12-21 as with the following amended paragraph:

This application also is related to U.S. application Serial No. ~~attorney dkt No. 25885-1754 and 25885-1754PC~~, 10/699,088 and International application Serial No. PCT/US03/34821 entitled "METHODS FOR PRODUCING POLYPEPTIDE-TAGGED COLLECTIONS AND CAPTURE SYSTEMS CONTAINING THE TAGGED POLYPEPTIDES," to U.S. application Serial No. ~~attorney dkt. nos. 25885-1759 and 25885-1759PC,~~ 10/699,114 and International application Serial No. PCT/US03/34693 each entitled "SYSTEMS FOR CAPTURE AND ANALYSIS OF BIOLOGICAL PARTICLES AND METHODS USING THE SYSTEMS", and to U.S. application Serial No. ~~attorney dkt. nos. 25885-1755PC,~~ 10/699,113 and International application Serial No. PCT/US03/34747, each entitled, "SELF-ASSEMBLING ARRAYS AND USES THEREOF", filed the same day herewith.

Please replace the paragraph beginning at page 2, line 22-24 as with the following amended paragraph:

The subject matter of each of the above-noted applications, provisional applications, published applications and ~~internaional~~ international applications is incorporated in its entirety by reference thereto.

Please replace the paragraph beginning at page 26, line 48 to page 27, line 10 as with the following amended paragraph:

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which the invention(s) belong. All patents, patent applications, published applications and publications, ~~Genbank~~ GENBANK sequences, websites and other published materials referred to throughout the entire disclosure herein, unless noted otherwise, are incorporated by reference in their entirety. In the event that there are a plurality of definitions for terms herein, those in this section prevail. Where reference is made to a URL or other such identifier or address, it is understood that such identifiers can change and particular information on the internet can come and go, but equivalent information is known and can be readily accessed, such as by

searching the internet and/or appropriate databases. Reference thereto evidences the availability and public dissemination of such information.

Please replace the paragraph beginning at page 36, line 9-14 as with the following amended paragraph:

As used herein, a conjugation reagent, such as a bifunctional or trifunctional reagent, refers to any chemical or biological compound or molecule that assists in the conjugation of two or more molecules. The conjugation reagent, such as a ~~binfunctional~~ bifunctional or trifunctional reagent, can be part of the linkage between the two or more molecules or facilitate the conjugation without becoming a physical part of the linkage.

Please replace the paragraph beginning at page 44, line 16-27 as with the following amended paragraph:

As used herein, the term "biopolymer" is a biological molecule, including macromolecules, composed of two or more monomeric subunits, or derivatives thereof, which are linked by a bond or a macromolecule. A biopolymer can be, for example, a polynucleotide, a polypeptide, a carbohydrate, or a lipid, or derivatives or combinations thereof, for example, a nucleic acid molecule containing a peptide nucleic acid portion or a glycoprotein, respectively. ~~Biopolymer~~ Biopolymers include, but are not limited to, nucleic acid, proteins, polysaccharides, lipids and other macromolecules. Nucleic acids include DNA, RNA, and fragments thereof. Nucleic acids can be derived from genomic DNA, RNA, mitochondrial nucleic acid, chloroplast nucleic acid and other organelles with separate genetic material.

Please replace the paragraph beginning at page 47, line 18 to page 48, line 10 as with the following amended paragraph:

As used herein, to hybridize under conditions of a specified stringency is used to describe the stability of hybrids formed between two single-stranded DNA fragments and refers to the conditions of ionic strength and temperature at which such hybrids are washed, following annealing under conditions of stringency less than or equal to that of the washing step. Typically high, medium and low stringency encompass the following conditions or equivalent conditions thereto:

1) high stringency: 0.1 x SSPE or SSC, 0.1% SDS, 65°C
2) medium stringency: 0.2 x SSPE or SSC, 0.1% SDS, 50°C
3) low stringency: 1.0 x SSPE or SSC, 0.1% SDS, 50°C.

Equivalent conditions refer to conditions that select for substantially the same percentage of mismatch in the resulting hybrids. Additions of ingredients, such as formamide, ~~Ficoll~~ FICOLL, and Denhardt's solution affect parameters such as the temperature under which the hybridization is conducted and the rate of the reaction. Thus, hybridization in 5 X SSC, in 20% formamide at 42°C is substantially the same as the conditions recited above hybridization under conditions of low stringency. The recipes for SSPE, SSC and Denhardt's and the preparation of deionized formamide are described, for example, in Sambrook *et al.* (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Chapter 8; see, Sambrook *et al.*, vol. 3, p. B.13, see, also, numerous catalogs that describe commonly used laboratory solutions). It is understood that equivalent stringencies can be achieved using alternative buffers, salts and temperatures.

Please replace the paragraph beginning at page 57, line 10-16 as with the following amended paragraph:

The binding partners are linked, such as cross-linked, to molecules [[andor]] and/or biological particles that are to be displayed. After linking the molecule and/or biological particle to each binding partner to produce conjugates, the resulting conjugates are contacted with the collection of capture agents to produce self-assembled arrays that display the molecules and/or biological particles. An exemplary self-assembling array is shown in Figure 1.

Please replace the paragraph beginning at page 66, line 10-20 as with the following amended paragraph:

Dispensing and immobilizing systems are widely available and well known (see, *e.g.*, systems available from Cartesian Systems, Irvine, CA, which has a system for printing on flat surfaces; from ~~Illumina~~ ILLUMINA, which employs the tips of fiber optic cables as supports; from TEXAS INSTRUMENTS, which has a surface plasmon resonance chip (*i.e.*, protein derivatized gold); inkjet systems, such as those from Microfab Technologies (Plano TX), ~~Incyte~~ INCYTE (Palo Alto, CA), ~~Protogene~~ PROTOGENE (Mountain View, CA), Packard BioSciences (Meriden CT) and other such systems for dispensing and immobilizing proteins to suitable support surfaces). Other systems such as blunt and quill pins, solenoid and piezo nanoliter dispensers, pintools and others also are contemplated.

Please replace the paragraph beginning at page 67, line 1-26 as with the following amended paragraph:

Supports that also are contemplated for use herein include fluorophore-containing or fluorophore-impregnated supports, such as microplates and beads (commercially available, for example, from ~~Amersham~~ AMERSHAM, Arlington Heights, IL; plastic scintillation beads from Nuclear Technology, Inc., San Carlos, CA and Packard, Meriden, CT, and colored bead-based supports (fluorescent particles encapsulated in microspheres) from ~~Luminex~~ LUMINEX Corporation, Austin, TX (see, International PCT application No. WO/0114589, which is based on U.S. application Serial No. 09/147,710; see International PCT application No. WO/0113119, which is U.S. application Serial No. 09/022,537). The microspheres from ~~Luminex~~ LUMINEX, for example, are internally color-coded by virtue of the encapsulation of fluorescent particles and can be provided as a liquid array. The capture agents, such as antibodies, are linked directly or indirectly by any suitable method and linkage or interaction to the surface of the bead and bound proteins can be identified by virtue of the color of the bead to which they are linked. Detection can be effected by any method, and can be combined with chromogenic or fluorescent detectors or reporters that result in a detectable change in the color of the microsphere (bead) by virtue of the colored reaction and color of the bead. Detection methods include, but are not limited to, methods including, ultraviolet-visible (UV-VIS) spectroscopy, infra-Red (IR) spectroscopy, fluorescence spectroscopy, fluorescence resonance energy transfer (FRET), NMR spectroscopy, circular dichroism (CD), mass spectrometry, other analytical methods, enzymatic assays for detection, antibody assays and other biological and/or chemical detection methods or any combination thereof.

Please replace the paragraph beginning at page 69, line 1-18 as with the following amended paragraph:

The preparation of and use of such supports are well known to those of skill in this art; there are many such materials and preparations thereof known. For example, naturally-occurring materials, such as agarose and cellulose, can be isolated from their respective sources, and processed according to known protocols, and synthetic materials can be prepared in accord with known protocols. These materials include, but are not limited to, inorganics, natural polymers, and synthetic polymers, including, but are not limited to: cellulose, cellulose derivatives, acrylic resins, glass, silica gels, polystyrene, gelatin, polyvinyl

pyrrolidone, co-polymers of vinyl and acrylamide, polystyrene cross-linked with divinylbenzene or the like (see, Merrifield (1964) *Biochemistry 3:*1385-1390), polyacrylamides, latex gels, polystyrene, dextran, polyacrylamides, rubber, silicon, plastics, nitrocellulose, celluloses, natural sponges, polystyrene, radiation grafted polymers, polyvinylidene ~~fluoride~~ difluoride (PVDF), and many others. Selection of the supports is governed, at least in part, by their physical and chemical properties, such as solubility, functional groups, mechanical stability, surface area swelling propensity, hydrophobic or hydrophilic properties and intended use.

Please replace the paragraph beginning at page 72, line 11-20 as with the following amended paragraph:

U.S. Patent No. 4,171,412 describes specific supports based on hydrophilic polymeric gels, generally of a macroporous character, which carry covalently bonded D-amino acids or peptides that contain D-amino acid units. The basic support is prepared by copolymerization of hydroxyalkyl esters or hydroxyalkylamides of acrylic and methacrylic acid with crosslinking acrylate or methacrylate comonomers are modified by the reaction with diamines, amino acids or dicarboxylic acids and the resulting carboxy terminal or amino terminal groups are condensed with D-analogs of amino acids or peptides. The peptide containing D- ~~aminoacids~~ amino acids also can be synthesized stepwise on the surface of the carrier.

Please replace the paragraph beginning at page 72, line 29 to page 73, line 3 as with the following amended paragraph:

Among the supports contemplated herein are those described in International PCT application Nos WO 00/04389, WO 00/04382 and WO 00/04390; KODAK film supports coated with a matrix material; see also, U.S. Patent Nos. 5,744,305 and 5,556,752 for other supports of interest. Also of interest are colored "beads," such as those from ~~Luminex~~ LUMINEX (Austin, TX).

Please replace the paragraph beginning at page 78, line 28 to page 79, line 21 as with the following amended paragraph:

Capture agents provided herein can be obtained by any method known to those of skill in the art. Such methods include, but are not limited to, purchase from commercial sources, synthetic preparation, isolation from complex mixtures and academic sources such as a gift from a collaborator. Purchase from commercial sources include, but are not limited

to, purchase from a biotechnology, chemical or specialty company such as via a catalog, phone or internet purchase; and purchase of a specifically designed molecules or biological particles, such as an oligonucleotide or polypeptide with a specific sequence. Synthetic preparation includes, but is not limited to, techniques such as solid-phase peptide syntheses using tBoc (Hackeng *et al. Protein Sci. 10(4):* 864-870 (2001)) or Fmoc chemistry (Wellings *et al. Methods Enzymol. 289:* 44-67 (1997)), which can optionally be automated using commercial systems such as the ~~Pioneer™~~ Pioneer and ABI 433A systems from ~~Applied Biosystems~~ APPLIED BIOSYSTEMS or the Apex 396 system from Advanced Chemtech; solid-phase oligonucleotide synthesis techniques, such as phosphoramidite techniques (Caruthers *et al. Gene Amplif. Anal. 3:* 1-26 (1983)), which can be optionally automated using commercial systems such as the ~~Expedite™~~ EXPEDITE 8909 from ~~Applied Biosystems~~ APPLIED BIOSYSTEMS or AKTA® ~~OligoPilot~~ OLIGOPILOT DNA/RNA synthesizer from ~~Amersham Biosciences~~ AMERSHAM BIOSCIENCES; and small molecule synthesis using methods well known to those with skill in the art. Isolation from a complex mixture includes, but is not limited to, chromatographic separation techniques, electrophoretic separations, immunological separations, hybridization techniques, growth and expression techniques and spectroscopic techniques.

Please replace the paragraph beginning at page 99, line 6-24 as with the following amended paragraph:

In silico methods can be used to determine capture agent - polypeptide tag pairs. Structural information (NMR and X-ray) is known for numerous immunoglobulins and is accessible, for example, at the Protein Databank (www.rcsb.org/pdb/) and ImMunoGeneTics (www.imgt.cnusc.fr:8104/home.html). Using one of a number of available Molecular Modeling programs such as ~~HyperChem~~ HYPERCHEM (Hypercube, Inc.), ~~InsightII~~ INSIGHTII(Molecular Simulations, Inc.), SpartanPro (Schrodinger, Inc.) ~~Sybyl~~ SYBYL (Tripos, Inc.) and ~~XtalView~~ XTALVIEW (Tripos, Inc.) the structural data can be manipulated in silico to identify potential molecules that can interact with the variable region of the antibody. The energy of interaction between the antibody and potential epitope can be determined using a molecular docking program such as DOCK, which is commercially available; see, also, *e.g.*, (www.cmpharm.ucsf.edu/kuntz/ dock.html), AutoDock (www.scripps.edu/pub/olson-web/doc/autodock/), IDock

(www.archive.ncsa.uiuc.edu/Vis/Projects/ Docker/) or SPIDeR (www.simbiosys.ca/sprout/eccc/spider.html). Once identified and the binding energy is determined in silico, polypeptides that constitute the tags can be synthesized or purchased commercially and tested in vitro for their specificity and affinity for the antibody in question.

Please replace the paragraph beginning at page 100, line 18 to page 101, line 2 as with the following amended paragraph:

In one exemplary embodiment, mice are immunized with a collection of peptide binding partners, for example as ~~diptheria~~ diphtheria toxin-6 mer peptide conjugates. Antibodies are raised against the collection of peptides. A library of hybridoma cells is then generated and clones are screened for their reactivity with individual peptides. Positive clones identify monoclonal antibodies which bind a selected peptide binding partner. The antibodies can be isolated by standard immunopurification techniques or by cloning methods such as by PCR with primers for conserved regions of the ~~anitbody~~ antibody structure. Once the antibody is isolated, the peptide or antigen responsible for the identification of the antibody is conjugated to a molecule and/or biological particle, as described below, and screened against the antibodies isolated above to determine whether the peptides or antigens retain their ability to be captured by the capture agent, thereby identifying a capture agent - binding partner pair.

Please replace the paragraph beginning at page 106, line 19 to page 107, line 4 as with the following amended paragraph:

For convenience and exemplification, the conjugates provided can be represented by the formula:

$$(BP)_s - (L)_q - (M)_p$$

wherein q is 0 or an integer of 1 up to n; s and p, which are the same or different, are integers of 1 up to m; and m and n, which are the same or different, are generally 1 or 2, but can be 2, 3, 4, 5, 6 or more as long as the resulting conjugate binds to a capture agent. L is an optional linker, BP is binding partner, M is molecule and/or biological particle and BP is linked either directly or indirectly via one or more linkers to M such that the resulting conjugate remains conjugated when bound to a capture agent. For example, where M is a biological particle such as a cell, each cell can have a plurality of receptors or other surface molecules to which a binding partner binds. In such instances, p can vary from conjugate to conjugate and also can not be readily ascertained. The stoichiometry of each conjugate is not ~~critial~~ critical to

practice of the method. Stoichiometry can be selected and controlled by methods known to those of skill in the art, such as empirically or by selecting appropriate concentrations of the binding partner and moiety to be tagged.

Please replace the paragraph beginning at page 108, line 15-29 as with the following amended paragraph:

The fusion proteins can be produced by recombinant expression of nucleic acids that encode the fusion protein. The formation of a fusion protein involves the placement of two separate coding sequences, such as genes or nucleotides sequences, one encoding the displayed molecule and the second encoding the binding partner, in sequential order in an appropriate cloning vector. Methods for creating an expression vector containing the displayed molecule and the binding partner are well known to those of skill in the art (see, *e.g.,* Sambrook et al. (1989) *Molecular Cloning: A Laboratory Manual*, [[Clod]] Cold Spring Harbor Laboratories, Cold Spring Harbor, New York). Additional methods for the formation of a fusion protein conjugate include, but are not limited to ligation of sequences resulting in linear tagged cDNA molecules; primer extension and PCR for binding partner incorporation; insertion by gene shuffling; recombination strategies; incorporation by transposases; and incorporation by splicing.

Please replace the paragraph beginning at page 109, line 30 to page 110, line 14 as with the following amended paragraph:

Several commercial kits are available for the formation of fusion proteins, which contain the displayed molecule fused to a second protein or nucleotide sequence, including, but not limited to, any of the polypeptides of SEQ ID Nos. 1-34. For example, the GFP Fusion TOPO® cloning vector and the pcDNA-DEST47 ~~Gateway™~~ Gateway vector are available from INVITROGEN (Carlsbad, CA) for the expression of a displayed protein fused to GFP; the pET-32a-c(+), the pET-44a-c(+) and the pET-41a-c(+) vectors are available from NOVAGEN (Madison, WI) for the expression of a protein fused to thioredoxin (SEQ ID No. 32), NusA (SEQ ID No. 29), a HSV tag (SEQ ID No. 5), Glutathione S-transferase and a His tag (SEQ ID No. 25); and the pShooter vectors from INVITROGEN (Carlsbad, CA) for the expression of a protein fused to a c-myc tag (SEQ ID No. 6). Further, custom designed and assembled genes and vectors, including those for fusion protein production, can be ordered and prepared by commercial sources, such as by SIGMA GENOSYS (The Woodlands, TX).

Please replace the paragraph beginning at page 111, line 25 to page 112, line 8 as with the following amended paragraph:

Cross-linking reactions involving molecules and binding partners, such as proteins, are generally reactive group reactions, such as side chain reactions, and are nucleophilic, resulting in a portion of the end of the cross-linker being displaced in the reaction (the leaving group). Nucleophilic attack is dependent on the pH, temperature and ionic strength of the cross-linking buffer. For example, when the buffer is one to two pH units below the pK_a of the reactive group, such as a side chain, the species is highly protonated and is most reactive. One to two pH units above the pK_a, the species is not protonated and not reactive. The majority of molecules and binding partners, such as proteins, have reactive groups, such as primary amines and free ~~sulfhydrals~~ sulfhydryls, available at the surface or terminus of the molecules or binding partner. These are the two most commonly used groups in molecular cross-linking strategies. Cross-linking strategies can also use carbohydrates, carboxyls or other reactive functional groups.

Please replace the paragraph beginning at page 115, line 2-13 as with the following amended paragraph:

Several methods are known to those skilled in the art for introducing thiols into molecules, such as polypeptides, or biological particles, including, but not limited to, the reduction of intrinsic disulfides, as well as the conversion of amine, aldehyde or carboxylic acid groups to thiol groups. For example, disulfide crosslinks of ~~cystines~~ cysteins in proteins can be reduced to cysteine residues by dithiothreitol (DTT), tris-(2-carboxyethyl)phosphine (TCEP) or tris-(2-cyanoethyl)phosphine. Reduction can result in loss of protein activity or specificity. Excess DTT should be carefully removed under conditions that prevent reformation of the disulfide, whereas excess TCEP usually does not need to be removed before carrying out the crosslinking reaction. TCEP also is stable at higher pH values than is the air-sensitive DTT reagent.

Please replace the paragraph beginning at page 157, line 12 to page 158, line 2 as with the following amended paragraph:

The combinations, kits, systems and methods provided herein allow for detection of the modulation of cellular apoptosis resulting from the interaction of a biological particle with displayed target molecules in a self-assembling array. Stains specific for cell viability, such as trypan blue or propidium iodide, can be used to determine cell viability after exposure

to a displayed molecule library on the self-assembled array (capture system). Necrotic cells are detected by intense propidium iodide staining of the cytoplasm, due to the complete disruption of the plasma membrane. ~~ApopNexin~~™ APOPNEXIN Kits (Serological Corp.) also are used to discriminate apoptotic from necrotic cells, and to label the progression of a cell through the various stages of apoptosis. As apoptosis progresses into the late-stage, the plasma membrane becomes permeable to DNA dyes such as propidium iodide, which enter the cell and stain yellow/orange.

Please replace the paragraph beginning at page 165, line 25 to page 166, line 2 as with the following amended paragraph:

For example, cell permeant caspase substrates such as PhiPhiLux® (ONCOIMMUNIN, Inc.); cell permeant caspase 3 and caspase 7 fluorogenic substrates from Molecular Probes; CaspSCREEN Apoptosis Detection Substrate (CHEMICON); and ~~CaspaTag™~~ CaspaTag Fluorescein Caspase Activity Kits (Serologicals Inc.) can all be used to monitor production and activity of the caspases. In addition, immunostains, such as anti-active caspase 3 monoclonal antibodies (BD PHARMINGEN), also are available for detection of apoptosis via the caspases.

Please replace the paragraph beginning at page 166, line 3-15 as with the following amended paragraph:

In normal cells, most of the phosphatidylserine (PS) contained in the plasma membrane is oriented towards the cytoplasmic side of the cell membrane. In early stage apoptosis, the cell undergoes surface membrane blebbing, cytoplasmic shrinkage, nuclear DNA fragmentation, chromatin condensation and PS translocation across the plasma membrane to the exposed outer surface of the cell. It is thought that the PS on the membrane surface identifies the cell as a target for destruction by the immune system. ~~ApopNexin™~~ APOPNEXIN Apoptosis Detection Kits (Serological Corp.) exploit this biochemical event using the annexin V protein labeled with either FITC or biotin. Annexin V is a calcium-dependent phospholipid binding protein with a high affinity for PS. In the presence of calcium, annexin V binds rapidly and specifically to PS and is visualized by flow cytometry or microscopy.

Please replace the paragraph beginning at page 166, line 15-31 as with the following amended paragraph:

Mitochondria have the ability to promote apoptosis through release of cytochrome C, which together with Apaf-1 and ATP forms a complex with pro-caspase 9, leading to activation of caspase 9 and the caspase cascade. Bax, and other Bcl-2 proteins, show structural similarities with pore-forming proteins. It has therefore been suggested that Bax can form a transmembrane pore across the outer mitochondrial membrane, leading to loss of membrane potential and efflux of cytochrome C and AIF (apoptosis inducing factor). Fluorescent probes of mitochondrial membrane potential, which drops in apoptotic cells, are available and include, MITOTRACKER Red, Rhodamine 123, and JC-1 (Molecular Probes); MITOLIGHT (CHEMICON); and the ~~MitoTag~~™ MITOTAG JC-1 Assay Kit (Serologicals Corp.). Anti-cytochrome C monoclonal antibodies with a conjugated enzyme or fluorophore also can be used to detect apoptosis. Additional assays for apoptosis stages such as chromatin condensation and fragmentation, are readily available for microscopic detection of DNA fragmentation.

Please replace the paragraph beginning at page 170, line 3-16 as with the following amended paragraph:

In another embodiment, TCR libraries are conjugated with the binding partners and displayed as such on the self-assembling array. Biological particles, such as antigen presenting cells (APCs) or recombinant cells that are modified to express peptides in the context of the major histocompatibility complex (MHC, class I or class II) on their surfaces, are "pulsed" or otherwise induced to express peptide epitopes in the context of major ~~histocompatability~~ histocompatibility complex (MHC), then exposed to the self-assembled array. Specific TCR-peptide MHC (pMHC) interactions bring APCs into contact with cognate, displayed TCRs. The interactions between the APCs and the self-assembled array (capture system) allows for visualization of components within the system including, but not limited to, specifically bound APCs, various fluorescently labeled secondary stains, and various fluorescently labeled, engineered cell-specific proteins.

Please replace the paragraph beginning at page 188, line 18-25 as with the following amended paragraph:

Non-natural amino acids that are modifications of natural amino acids in the side chain functionality, such that the methylene groups of the side chain of the natural amino

acids have been substituted by imino groups or divalent non-carbon atoms or, alternatively, methyl groups have been substituted by amino groups, hydroxyl groups or thiol groups, so as to add ability to form hydrogen bonds or to reduce their hydrophobic properties (*e.g.* leucine to 2-aminoethylcysteine, or ~~isolecine~~ isoleucine to o-methylthreonine).

Please replace the paragraph beginning at page 191, line 19 to page 192, line 6 as with the following amended paragraph:

Non-naturally occurring amino acids can be ranked for antigenicity using methods applied to the naturally occurring amino acids, for example by testing sequences against antisera or libraries of antibodies (described herein) and can be ranked along-side naturally occurring amino acids. For example, a ~~representive~~ representative set of polypeptides composed of non-naturally occurring amino acids and/or a combination of non-naturally occurring and naturally occurring amino acids of a chosen polypeptide length can be used to immunize animals. Based on the subset of polypeptides injected which are antigenic and non-antigenic, amino acids are identified which either are more likely to be present in antigenic polypeptides or are more likely to be present on non-antigenic polypeptides. The likelihood of a amino acid's presence in antigenic polypeptide gives an observed antigenic ranking. Some ~~non-ntural~~ non-natural amino acids are very structurally similar to naturally occurring amino acids and to other non-naturally occurring amino acids. This similarity can be factored in to provide antigenicity rankings based on these similarities. Non-naturally occurring amino acids can also be assigned a similarity ranking for use with the methods as described, based on their structural and functional similarity to each other and to naturally occurring amino acids.

Please replace the paragraph beginning at page 192, line 8-16 as with the following amended paragraph:

Once the polypeptides are designed, any of the subsets of polypeptides ~~desrcibed~~ described herein can be generated by standard methods known in the art. The ~~petides~~ peptides can be chemically synthesized by standard and/or combinatorial chemistry. ~~polypeptides~~ Polypeptides can also be synthesized using recombinant means such as by expression of nucleic acids encoding the polypeptide sequences. For recombinant expression, the polypeptides are limited to the 20 naturally occurring amino acids and additionally non-naturally occurring amino acids where the expression organism of choice has been genetically engineered to generate such modifications.

Please replace the paragraph beginning at page 197, line 14-27 as with the following amended paragraph:

High affinity and high specificity antibodies for the array were identified by screening a randomly selected collection of individual hybridoma cells against a phage display library expressing a random collection of peptide epitopes. The hybridoma cells were created by fusion of spleenocytes isolated from a naive (non-immunized) mouse with myeloma cells. After a stable culture was generated, approximately 10-30,000 individual cell clones (monoclonals) were isolated and grown separately in 96-well plates. The culture supernatants from this collection were screened by ELISA with an anti-IgG antibody to identify cultures secreting significant amounts of antibody. Cultures with low antibody production were discontinued. Antibodies from this monoclonal collection were separated from culture supernatants using ~~HiTrap~~ HITRAP Protein G- columns using the AKTA® Prime chromatography system following the manufacturer's protocol (AP Biotech).

Please replace the paragraph beginning at page 198, line 12-19 as with the following amended paragraph:

The wells were incubated at 37°C for 1 hour followed by 5 washes with 1X TBS-T (1 minute per wash) for round 1. The bound phage were eluted by addition of 100 μl of 0.1 M glycine, pH 2.2. This eluate was transferred into an ~~Eppendorf~~ EPPENDORF tube, followed by addition of 10 μl Tris, pH 8.0 to the same ~~Eppendorf~~ EPPENDORF tube. The glycine and Tris steps were repeated once more and this solution was now the OUTPUT. The OUTPUT from the first round was now to be used as INPUT for the second round.

Please replace the paragraph beginning at page 198, line 20-28 as with the following amended paragraph:

The grown ER2738 cells were centrifuged at 3500 rpm for 15 min and the cells resuspended in 1/20 of the original volume (1 ml) using Min A salts. One hundred microliters of the cells suspension was aliquoted into 15 ml Falcon tubes to which the OUTPUT (220 μl) was added and incubated at 37°C for 30 min. The volume was increased to 1.0 ml with 2X YT (add 680 μl 2X YT) and incubated at 30°C for 4 hours. The cells were spun at 8000 rpm for 15 min and the supernatants were transferred to ~~Eppendorf~~ EPPENDORF for use the next day as INPUT. These solutions were stored at 4°C.

Please replace the paragraph beginning at page 202, line 1-5 as with the following amended paragraph:

Eight positive phage clones were picked and added to a 96-deep well plate that contained 100 µl of E. coli 2738 cells. The plate was incubated at 37°C for 30 min followed by addition of 900 µl of 2X YT media and an additional incubation at 37°C for 4 hour. This plate was sent to MJ Research (Waltham, [[CA)]] MA) for sequencing.

Please replace the paragraph beginning at page 203, line 20 to page 204, line 12 as with the following amended paragraph:

To demonstrate the functioning of the methods herein, capture antibodies, specific, for example, for various peptide epitopes, such as the human influenza virus hemagglutinin (HA) protein epitope, which has the amino acid sequence YPYDVPDYA (SEQ ID No. 4), were used to tag, for example, scFvs. For example, an scFv with antigen specificity for human fibronectin (HFN) was tagged with an HA epitope, thus generating a molecule (HA-HFN), which was recognized by an antibody specific for the HA peptide and which has antigen specificity of HFN. After depositing various concentrations of the capture antibodies (from 800 µg/ml to 200 µg/ml), including anti-HA tag capture antibodies, onto a glass slide coated with a surface for capturing proteins, such as a nitrocellulose-coated slide (~~FAST~~™ FAST, Schleicher and Schuell), they were allowed to bind at ambient temperature and humidity of 50 to 60%. After binding, slides with deposited anti-HA capture antibodies were blocked with a protein-containing solution such as ~~Blocker~~™ ~~BSA~~ Blocker BSA (PIERCE) diluted to 1X in phosphate-buffered saline (PBS) with TWEEN-20 (polyoxyethylenesorbitan monolaurate; SIGMA) added to a final concentration of 0.05% (vol:vol) or with a 3% non-fat milk in the same buffer to eliminate background signal generated by non-specific protein binding to the membrane. For subsequent description contained herein PBS with 0.05% (vol:vol) TWEEN-20 is referred to as PBS-T. Blocking times can be varied from 60 min at ambient temperature to longer hours at ambient temperature or at 4°C, for example. Incubation temperatures for all subsequent steps can be varied from ambient temperature to about 37°C. In all instances, the precise conditions are determined empirically.

Please replace the paragraph beginning at page 204, line 25 to page 205, line 6 as with the following amended paragraph:

Membranes with deposited anti-HA capture antibodies and bound HA-HFN scFv then were incubated with, for purposes of demonstration, biotinylated human fibronectin (Bio-

HFN), which is an antigen that can be recognized by the capture HA-HFN scFv. Bio-HFN was serially diluted (e.g., from 1 to 10 μg/ml) in BBSA-T. The resulting membranes were washed as before and then were incubated with Neutravidin•HRPO (PIERCE) diluted 1 in 10000 in BBSA-T. The resulting slides were washed as before, rinsed with PBS and developed with a 1:1 mixture of freshly prepared ~~Supersignal~~™ SUPERSIGNAL ELISA Femto Stable Peroxide Solution and ~~Supersignal~~™ SUPERSIGNAL ELISA Femto Lumino Enhancer Solution (PIERCE), and then imaged using an imaging system, such as, for example, a KODAK Image Station 440CF or IS1000 or other such imaging system. A small volume of the ~~Supersignal~~™ SUPERSIGNAL solution was plated on the platen of the image station.

Please replace the paragraph beginning at page 205, line 26 to page 206, line 2 as with the following amended paragraph:

Capture agents (~~CytoSets~~™ CytoSets capture antibodies) were printed with an inkjet printer (CANON model BJC 8200 color inkjet) modified for this application. The six color ink cartridges were first removed from the print head. One-milliliter pipette tips then were cut to fit, in a sealed fashion, over the inkpad reservoir wells in the print head. Various concentrations of capture antibodies, in glycerol, then were pipetted into the pipette tips which were seated on the inkpad reservoirs (typically the pad for the black ink reservoir was used).

Please replace the paragraph beginning at page 206, line 3-14 as with the following amended paragraph:

For generation of printed images using the modified printer, MICROSOFT POWERPOINT was used to create various on-screen images in black-and-white. The images then were printed onto nitrocellulose paper (Schleicher and Schuell (S&S) PROTRAN BA85, pore size 0.45 μm, VWR catalog # 10402588, lot # CF0628-1) which was cut to fit and taped over the center of an 8.5 x 11 inch piece of printer paper. This two-paper set was hand fed into the printer immediately prior to printing. After printing of the image, the antibodies were dried at ambient temperature for 30 min. The nitrocellulose was removed from the printer paper, and processed as described below (see Basic protocol for antibody and antigen incubations: ~~FAST~~™FAST slides and nitrocellulose filters printed with ~~CytoSets~~™ CytoSets capture antibodies).

Please replace the paragraph beginning at page 206, line 16 to page 207, line 7 as with the following amended paragraph:

Capture agent antibody dilutions were printed onto nitrocellulose slides (Schleicher and Schuell ~~FAST~~™FAST slides; VWR catalog # 10484182, lot # EMDZ018) using a pin-printer-style arrayer (MicroSys 5100; Cartesian Technologies; TeleChem ~~ArrayIt~~™ ARRAYIT Chipmaker 2 microspotting pins, catalog # CMP2). Printing was performed using the manufacturer's printing software program (Cartesian Technologies' AxSys version 1, 7, 0, 79) and a single pin (for some experiments), or four pins (for some experiments). Typical print program parameters were as follows: source well dwell time 3 sec; touch-off 16 times; microspots printed at 0.5 mm pitch; pins down speed to slide (start at 10 mm/sec, top at 20 mm/sec, acceleration at 1000 mm/sec^2); slide dwell time 5 millisec; wash cycle (2 moves + 5 mm in rinse tank; vacuum dry 5 sec); vacuum dry 5 sec at end. Array patterns were pre-programmed (in-house) to suit a particular array configuration. In many cases, replicate arrays were printed onto a single slide, allowing subsequent analyses of multiple analyte parameters (as one example) to be performed on a single printed slide. This in turn maximized the amount of experimental data generated from such slides. Microtiter plates (96-well for most experiments, 384-well for some experiments) containing capture antibody dilutions were loaded into the array printer for printing onto the slides. Based on the reported print volume (post-touch-off, see above) of 1 nl/microspot for the Chipmaker 2 pins, the capture antibody concentrations contained in the printed microspots typically ranged from 800 to 6 pg/microspot.

Please replace the paragraph beginning at page 214, line 13 to page 215, line 2 as with the following amended paragraph:

Carboxylate-modified polystyrene beads (SIGMA, Catalog No. CLB-4) were washed twice with Washing buffer (25mM MES, pH 6.1 containing 0.01% TWEEN-20) and resuspended in 10 volumes of Washing buffer. EDC (1-Ethyl-3-[3-dimethylaminopropyl] carbodiimide ~~Hydrocloride)~~ Hydrochloride) was added to activate the beads at a final concentration of 1mM. The beads were incubated at ambient temperature for 15 min with slow mixing. The beads were washed and following resuspension in 10 volumes of Washing buffer, a 1mg/ ml anti-HA11 antibody solution was added to the beads (1/10th the volume of bead suspension) and the antibody allowed to bind to the beads at ambient temperature for 2 hours with slow mixing. The reaction was stopped by addition of Glycine at 50 mM final

concentration and incubation at ambient temperature for 30 min. The beads were washed twice with Washing buffer and then resuspended in 10 volumes of Storage buffer (Phosphate-buffered saline containing 1% BSA and 0.1% TWEEN-20).

Please replace the paragraph beginning at page 216, line 7-14 as with the following amended paragraph:

The wells in the plate were blocked by addition of Blocking buffer (1% BSA in PBS containing 0.1% TWEEN-20) and incubated at 37°C for 60 min. Various dilutions of the antibody conjugated beads in Blocking buffer were added to the wells and the plate incubated at 37°C for 60 min. The plate was washed thrice with PBS-T, followed by incubation with the goat anti-mouse IgG-HRP conjugate at 37°C for 60 min. The plate was washed as before and developed with ~~Luminol~~ LUMINOL and imaged on a KODAK IS1000.

Please replace the paragraph beginning at page 216, line 16-21 as with the following amended paragraph:

The anti-HA-11 antibody beads bound to the peptide spots corresponding to the HA-11 peptide. The antibody bound to the other peptide spots with much lower or insignificant binding (as measured [[bu]] by the luminosity). The positive control spots (mouse IgG and Mouse IgG-HRP) gave detectable signal, similar to the level of signal with the HA-11 peptide spot.

Please replace the paragraph beginning at page 219, line 28 to page 220, line 2 as with the following amended paragraph:

The selected clones were grown for 2 weeks and the medium was used for analysis of antibody class and for specificity of binding to polypeptides by performing the assay described above. IgG was isotyped using Isotype mouse isotyping kits ~~(Roche).~~ (ROCHE). The antibody from the supernatant was purified using Protein G affinity chromatography and stored in liquid nitrogen.